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## FULFIL

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## FULFIL an unmet need in COPD

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## **FULFIL an unmet need in COPD**

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To the Editor,

We read with interest the recent data from the FULFIL trial which showed that for both co-primary end points, triple therapy comprising inhaled corticosteroid with long acting beta-agonist and muscarinic antagonist (ICS/LABA/LAMA) was superior to twice daily dual therapy (ICS/LABA) after 24 weeks in patients with COPD (1), confirming the known benefits of dual verses single long acting bronchodilator therapy(2). It was nonetheless impressive that for trough FEV1 at 24 weeks, the mean difference of 171ml was not only statistically significant but also exceeded the minimal clinical important difference (MCID) of 100ml(3), suggesting that the impact of single inhaler triple therapy was clinically relevant. The same was not however true for SGRQ score where the mean difference of 2.2, while statistically significant, was less than the MCID of 4.0. Nonetheless there were 35% significantly fewer exacerbations at the same time point. A real life observational study with time dependent analysis in 2853 patients with COPD over 4.65 years showed a 29% significant reduction in exacerbations requiring oral corticosteroids and 15% significantly fewer hospital admissions conferred by taking once daily tiotropium in addition to twice daily ICS/LABA as separate inhalers (4). Moreover such triple therapy was associated with 35% significantly lower all cause mortality. The question remains as to whether equally impressive differences would be seen when comparing single inhalers containing ICS/LABA/LAMA and LABA/LAMA, particularly since LABA/LAMA has been shown to be superior to ICS/LABA (5). This will be important to know since combinations containing ICS are

more likely to be associated with pneumonia, especially with fluticasone furoate which has prolonged lung retention (6).

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## References

1. Lipson DA, Barnacle H, Birk R, Brealey N, Locantore N, Lomas DA, Ludwig-Sengpiel A, Mohindra R, Tabberer M, Zhu CQ, Pascoe SJ. FULFIL Trial: Once-Daily Triple Therapy in Patients with Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med* 2017;10.1164/rccm.201703-0449OC.
2. Buhl R, Maltais F, Abrahams R, Bjermer L, Derom E, Ferguson G, Flezar M, Hebert J, McGarvey L, Pizzichini E, Reid J, Veale A, Gronke L, Hamilton A, Korducki L, Tetzlaff K, Waitere-Wijker S, Watz H, Bateman E. Tiotropium and olodaterol fixed-dose combination versus mono-components in COPD (GOLD 2-4). *Eur Respir J* 2015; 45: 969-979.
3. Jones PW, Beeh KM, Chapman KR, Decramer M, Mahler DA, Wedzicha JA. Minimal clinically important differences in pharmacological trials. *Am J Respir Crit Care Med* 2014; 189: 250-255.
4. Short PM, Williamson PA, Elder DH, Lipworth SI, Schembri S, Lipworth BJ. The impact of tiotropium on mortality and exacerbations when added to inhaled corticosteroids and long-acting beta-agonist therapy in COPD. *Chest* 2012; 141: 81-86.
5. Wedzicha JA, Banerji D, Chapman KR, Vestbo J, Roche N, Ayers RT, Thach C, Fogel R, Patalano F, Vogelmeier CF, Investigators F. Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD. *N Engl J Med* 2016;10.1056/NEJMoa1516385.
6. Allen A, Bareille PJ, Rousell VM. Fluticasone furoate, a novel inhaled corticosteroid, demonstrates prolonged lung absorption kinetics in man

compared with inhaled fluticasone propionate. *Clin Pharmacokinet* 2013; 52: 37-42.

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